


## CASE REPORT

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# A rare case of lipid pneumonia attributed to amiodarone

Ilektra Voulgareli<sup>\*</sup> , Alexandra Chronaiou, Dionisios Tsoukalas and George Tsoukalas

### Abstract

We report a case of endogenous lipid pneumonia secondary to long-term use of amiodarone ( $\geq 30$  years) for atrial fibrillation in a 76-year-old Caucasian woman, presenting with cough and dyspnea. Endogenous Lipoid pneumonia is a rare underdiagnosed condition more prevalent in adults. It is usually asymptomatic and a diagnosis is generally made in patients who have become clinically unstable or when an abnormal lung shadow is found on a chest X-ray. In the case here described it was diagnosed by fiberoptic bronchoscopy with bronchoalveolar lavage (BALF) where fat-laden macrophages (oil red O stain) were identified. Since a history of use of oil-based products had been ruled out, amiodarone was deemed to be the most likely cause of lipid pneumonia. The patient was managed with the replacement of amiodarone with digoxin and treated with oral prednisolone. The patient has remained clinically stable with radiological improvement during a follow-up of two years.

**Keywords:** Endogenous lipid pneumonia, Amiodarone, Bronchoalveolar lavage, Prednisolone treatment

### Introduction

Endogenous lipid pneumonia is an uncommon clinical condition, more prevalent in adult age, but generally underdiagnosed. It can be associated with bronchial obstruction [1], systemic diseases such as rheumatoid arthritis, Hodgkin's lymphoma, and Wegener's granulomatosis or it can be idiopathic [2]. Here we report the case of a 76-year-old woman who was diagnosed with endogenous lipid pneumonia attributed to chronic use of amiodarone (30 years) and successfully treated with discontinuation of amiodarone and prescription of prednisolone. Amiodarone was replaced with digoxin. Most reported cases of lipid pneumonia diagnosed as exogenous lipid pneumonia are due to either aspiration or inhalation of mineral or vegetable oils [3, 11]. Lipid pneumonia occurs mostly in the elderly and in children with developmental disabilities, presumably because these groups are more prone to aspiration [15].

### Case report

A 76-year-old Caucasian female attended our pulmonology outpatient clinic with a four-week history of cough with mucous-purulent sputum and dyspnea. The patient

was a nonsmoker and had worked for a few years in a cotton factory. Her past medical history was negative for any contact with substances known to be associated with lipid pneumonia. She had not travelled recently and had no pets. She had been treated for atrial fibrillation with amiodarone (200 mg OD) for 30 years, systemic hypertension, diabetes mellitus type II and hypothyroidism. Physical examination revealed a well built and nourished patient with pulse rate 69 per minute and blood pressure 110/70 mmHg. Vital signs were within normal range with SpO<sub>2</sub> of 95% in room air. Her physical examination revealed bibasal lung crackles, but no evidence of pallor, icterus, cyanosis, clubbing or lymphadenopathy. Her blood work-up was within normal range. Pulmonary function testing demonstrated moderate restrictive lung disease and a decreased diffusion capacity. (see Table 1).

Since chest X-ray showed bilateral infiltrates, a high resolution computed tomography (HRCT) was conducted. The latter revealed areas of ground glass appearance significantly in the lower lobes of both lungs and airspace consolidations were seen as well (Fig. 1, [a], [b]). The shadows improved 2 years later (Fig. 1, [c]).

\* Correspondence: [ilektravoul@gmail.com](mailto:ilektravoul@gmail.com)

Department of Pneumology, Sotiria Hospital, Athens, Greece



**Table 1** Selected pulmonary function test results

	Observed	Predicted	Predicted (%)
Forced vital capacity (FVC)	2.32 L	2.59 L	90
Forced expiratory volume in 1 s (FEV1)	1.27 L	1.97 L	65
FEV1/FVC (%)	73	76	96
Inspiratory capacity	1.49 L	2.04 L	73
Total lung capacity	4.22 L	4.75 L	89
Residual volume	1.97 L	2.13 L	92
DLCO corrected for hemoglobin	10.71	19.48	55

Tests of pulmonary function indicating moderate restrictive pulmonary disease and a marked defect diffusing capacity. There was no improvement with inhaled bronchodilators (data not shown)

DLCO Diffusing capacity of the lung for carbon monoxide

Radiologically, differential diagnosis included atypical pneumonia, interstitial lung disease and tuberculosis was ruled out. The patient underwent fiberoptic bronchoscopy for bronchial wash and bronchoalveolar lavage (BALF) was collected for immunological studies as well. The bronchial washings were sent for smear for acid fast bacilli and cytological examination. No microorganisms were isolated by 48bacteriological examination and no malignant cells were found.

The total cell count of the BALF was 287,500/ml. The cells consisted of macrophages (64%), lymphocytes (31%), neutrophils (3%), and eosinophils (2%). The evaluation of BALF with specific staining and coloration showed the presence of fat-laden macrophages (oil red O stain). Figure 2 [a], [b] Extracellular oily droplets were found on a sputum cytology examination. These findings were suggestive of lipid pneumonia.

The patient had never aspirated or inhaled mineral or vegetable oils and she had never used petroleum jelly intranasally or extra-nasally as a decongestant. However, it is described in the literature that chronic use of amiodarone can cause endogenous lipid pneumonia (phospholipidosis) [17]. Amiodarone, as an amphiphilic cationic compound, interferes with the movement of

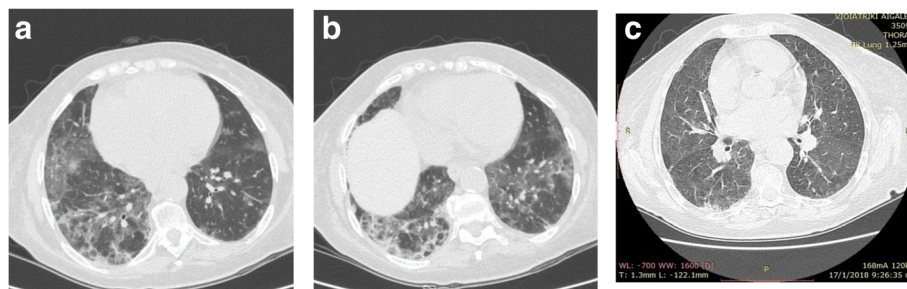
phospholipids across intracellular membranes and inhibits phospholipid catabolism through its potent inhibitory effect on lysosomal phospholipase 2. Drug-induced phospholipidosis assumes the form of a ‘foamy cell’ response.

In our case, the patient had been taking amiodarone (200 mg OD) for 30 years which was considered the most likely cause. It was therefore discontinued and replaced with digoxin (0.25 mg OD) for the treatment of atrial fibrillation. She was also started on oral prednisolone (20 mg OD) which was gradually tapered over a period of six months.

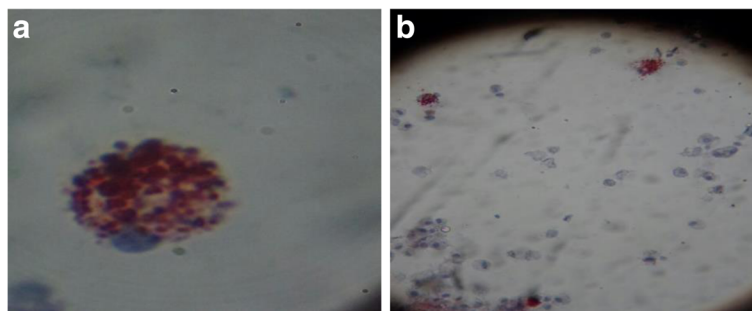
**Discussion**

Lipid pneumonia can be classified into endogenous lipid and exogenous lipid pneumonia [2, 5, 6]. Compared to exogenous lipid pneumonia, endogenous lipid pneumonia is rarer and its etiology, which is not clear, may be associated with metabolic or secretory abnormalities of cholesterol in the alveolar epithelial tissue and excessive release of lipids uptaken by histiocytes [2]. It is considered a chronic foreign body reaction to fat, characterized by lipid-laden macrophages [5] and is usually associated with bronchial obstruction [1]. Additionally, endogenous lipid pneumonia can be associated with systemic diseases such as rheumatoid arthritis, Hodgkin’s lymphoma, and Wegener’s granulomatosis. It can also be idiopathic and the pathogenes is unknown [2]. In the present case report there was no history of use of oil-based products so a diagnosis of endogenous lipid pneumonia was more likely in the absence of systemic diseases or obstructive changes on the imaging of the lungs. Since it is described in the literature that chronic use of amiodarone can cause endogenous lipid pneumonia it was deemed that this could be the agent responsible for the patient’s condition [15].

Amiodarone and its metabolites can produce lung damage directly through a cytotoxic effect and indirectly via an immunological reaction. Amiodarone may induce the production of toxic oxygen radicals, which can



**Fig. 1** Computed tomography images of a 76-year-old female with lipid pneumonia revealed ground-glass opacities and bronchiectasis in both lungs (a), (b). The shadows improved 2 years later (c)



**Fig. 2 a, b** The bronchoalveolar fluid examination in a 76-year-old female with lipid pneumonia. Oil phagocytosis by alveolar macrophages was observed under a microscope with Oil Red staining

directly damage cells. In addition, amiodarone appears to promote the accumulation of phospholipids in tissues. There is hyperplasia of type II pneumocytes and a widening of alveolar septae with a cellular inflammatory infiltrate and varying degrees of interstitial fibrosis [18]. On light microscopy, vacuolization of the cytoplasm was seen in alveolar pneumocytes, bronchial epithelial cells and endothelial cells [16]. The typical features and diagnosis of the lipid pneumonia depend on the presence of lipid-laden macrophages (the so-called ‘foamy cells’) in respiratory samples such as sputum, bronchoalveolar lavage fluid (BALF) or fine-needle aspiration (FNA) cytology/biopsy from lung lesions and of course on a high index of suspicion [2, 4, 7–9].

The usual course includes an insidious onset and non-specific respiratory symptoms such as dyspnea and/or cough. Rarely, it may present itself as an acute respiratory illness [6, 7, 9, 10] even with hemoptysis [13].

Radiological findings are diverse and may mimic carcinoma, acute or chronic pneumonia, ARDS, or a localized granuloma. High-resolution computed tomography (HRCT) is the best imaging modality for the diagnosis of lipid pneumonia. However, the radiological manifestations of the disease can be indistinguishable from pneumonia, lung cancer or/ and interstitial lung diseases [12]. In the literature it has also been reported that CT scan and magnetic resonance imaging can detect fat within pulmonary tissue. The most commonly described feature is alveolar consolidations of low attenuation values, ground glass opacities with a thickening of intralobular septa (‘crazy-paving’ pattern), or alveolar nodules [2, 6–8, 11].

Treatment of lipid pneumonia is not well studied and experiences are only limited to case reports. Some authors have suggested the use of systemic corticosteroids in order to slow the inflammatory response.

Nevertheless, corticosteroids may not be used routinely and may only be used if the lung injury is severe and ongoing. Some authors have described resection of the most involved lung segments while others the use of

immunoglobins or whole lung-lavages [2, 4, 7–9]. Our patient responded well to oral corticosteroids and her clinical conditions improved during a follow-up of two years.

### Conclusion

In conclusion, endogenous lipid pneumonia is very uncommon and in this case the diagnosis was attributed to the long-term use of amiodarone.

Lipoid pneumonia was confirmed by BALF (bronchoalveolar lavage) where foamy macrophages positive in Oil-red-O staining were found [14]. Withdrawal of the suspected agent and a trial of oral corticosteroids were the mainstay of our treatment. If undetected, lipid pneumonia can insidiously or symptomatically lead to pulmonary fibrosis and end-stage lung disease.

### Abbreviations

ARDS: Acute Respiratory Distress Syndrome; BALF: bronchoalveolar lavage; DLCO: Diffusing capacity of the lung for carbon monoxide; FNA: Fine Needle Aspiration; HRCT: High Resolution Computed Tomography

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### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on request.

### Authors’ contributions

The manuscript was prepared for submission by IV and AV. The final version of the manuscript was approved by all authors prior to submission.

### Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying data.

### Competing interests

The authors declare that they have no competing interests.

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